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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/926,234	10/22/2001	Maria Marino	214038US0PCT	2544

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	17

DATE MAILED: 06/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,234	MARINO ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3* is/are rejected.

7)☒ Claim(s) *1 and 2* is/are objected to.

8)☑ Claim(s) *1-3* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4) ☐ Interview Summary (PTO-413) Paper No(s) _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 21 December 2001 (Paper No. 3) has been entered in full.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-3, drawn to a peptide comprising SEQ ID NO: 1 and a method of treating a patient suffering from Multiple Sclerosis in Paper No. 13 (20 March 2003) is acknowledged. The traversal is on the ground(s) that the Office has not applied the same standard of unity of invention as the International Preliminary Examination Authority. Applicant argues that the Authority did not take the position that unity of invention was lacking in the International application and examined all claims together. Applicant indicates that the International Authority found the invention to possess novelty and inventive step. Applicant asserts that a search of all the claims would not impose a serious burden on the Office.

This is not found persuasive. Claims 1-3 will be examined together in the instant application, however, only to the extent that they read upon SEQ ID NO: 1. Although the International Preliminary Examination Authority appears to have examined all the amino acid sequences recited in the claims, the instant application has been filed as a national stage application under 35 U.S.C. 371. According to Rule 1.499, if the examiner finds that a national stage application lacks unity of invention under § 1.475, the examiner may require the applicant to elect an invention to which the claims are restricted. As discussed in the previous Office Action, claims 1-3 broadly encompass the amino acid sequences of 4 different peptides. The amino acid sequences of SEQ ID NOs: 1-4 are composed of different amino acids and are

structurally and functionally unrelated to one another. Therefore, these protein sequences are not linked under PCT Rule 13.1. In the response of 20 March 2003 (Paper No. 13), Applicant has not specifically explained the special technical features shared by these sequences and why they should be rejoined to each other. Additionally, each of SEQ ID NOs: 1-4 is a unique sequence, requiring a unique search of the prior art. Searching all of the sequences in a single patent application would provide an undue search burden on the examiner and the USPTO's resources because of the non-coextensive nature of these searches.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-3 are under consideration in the instant application as they read upon the peptide of SEQ ID NO: 1.

Claim Objections

1. Claims 1-3 are objected to because of the following informalities:

1a. Claims 1-3 recite a non-elected SEQ ID NOs.

1b. The term "pharmaceutical" in claim 2, line 14 should be changed to "pharmaceutically". Appropriate correction is required.

Information Disclosure Statement

2. The information disclosure statement filed 15 January 2002 (Paper No. 9) fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Brocke et al. and Karin et al. were not attached to the PTO-1449.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 3 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 3 is directed to a method of treating a patient suffering from Multiple Sclerosis, said method comprising administering to a patient in need thereof an effective amount of a peptide compound comprising R-Asn-Gly-Val-Gly-His-Gly-Phe-Gly-Asn-Gly-Val-Gly-Pro-Gly-Thr-Gly-Pro-Gly-Ser-Gly-R' (SEQ ID NO: 1) where R is H- or $COCH_3$ and R' is COOH or $CONH_2$ and each amino acid has a D or L conformation.

The specification teaches that the *in vivo* activity of the peptide of SEQ ID NO: 1 (formula 1) was evaluated on groups of SJL female mice, used at the age of 6-15 weeks. The specification also discloses that this strain of mice has been genetically selected for its ability to develop experimental allergic encephalitis (EAE) (pg 10, lines 26-30). The specification teaches that two groups of mice are immunized intraperitoneally with the peptide compound of formula I or II (pg 11, lines 1-5). The specification further discloses that after 2 weeks, EAE is induced all groups (including control) by challenge with P81-100 and mice are observed daily for clinical signs of EAE (pg 11, lines 8-22). Finally, the specification teaches that mice treated with the peptide of SEQ ID NO: 1 (formula 1) did not develop EAE (pg 12, lines 7-12; Table 1).

Although the specification discloses that the *inducement of EAE* can be prevented by vaccination with the peptide of formula I, the specification does not teach treating subjects suffering from EAE by administration of the chemically modified peptide of SEQ ID NO: 1 (formula I). Undue experimentation would be required of the skilled artisan to treat a patient suffering from Multiple Sclerosis (MS) by administering to the patient the peptide of SEQ ID NO: 1. A large quantity of experimentation would be required by one skilled in the art to determine the optimal dosage, duration, and route of administration of the peptide of SEQ ID NO: 1 for treatment of MS. The experiment in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Additionally, as was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). The present invention is unpredictable and complex wherein one skilled in the art may not necessarily treat MS by administering the peptide of SEQ ID NO: 1.

Furthermore, relevant literature teaches that in contrast to the successfully introduced and established immunomodulatory therapies, there are a number of therapeutic failures (abstract; entire article, Wiendl et al., BioDrugs 16(3): 183-200, 2002). Wiendl et al. review MS trials that failed or were discontinued, including cytokine modulators, immunosuppressive agents, and T cell and T-cell receptor therapies, among others. Wiendl et al. indicate that theoretically

promising agents may increase disease activity (such as lenercept and infliximab) or may be associated with unforeseen adverse effects (roquinimex) (pg 197, ¶ 3). Wiendel et al. also disclose that short-term favorable trends may reverse with prolonged follow-up (sulfasalazine). Therefore, with evidence indicating that not all MS therapeutic treatments are successful, one skilled in the art would not be able to predict the claimed method of administering the peptide of SEQ ID NO: 1 to a patient suffering from MS would actually treat MS.

Due to the large quantity of experimentation necessary to determine the optimal dosage, duration, and route of administration of the peptide of interest and to treat a patient *suffering from MS* by administering the peptide of SEQ ID NO: 1, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of the administration of the peptide of SEQ ID NO: 1 to a patient already suffering from MS, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure (EAE and peptide analogues):

Marino et al. Eur J Immunol 29 : 2560-2566, 1999.

Marino et al. Mol Immunol 37(16) : 951-960, 2000.

Karin et al. J Exp Med 180(6) : 2227-22367, 1994.

Samson et al. J Immunol 155(5) : 2737-2746, 1995.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
May 28, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER